

Attorney's Docket No. TAN-345
MAIL STOP AMENDMENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:) Group Art Unit: 1634

IMAI) Examiner: D. Cho

Serial No.: 10/511,910)

Filed: October 20, 2004)

For: **A METHOD FOR DETECTION OF RHEUMATOID ARTHRITIS BY
DETECTING UPREGULATION OF EXPRESSION OF WNT**

DECLARATION UNDER 37 C.F.R. § 1.132

I, Kazushi IMAI hereby declare as follows:

1. I am the inventor of the captioned application and am familiar with the subject matter of the captioned application and with the Office Action mailed on November 27, 2006.
2. The information contained in the disclosure of the captioned application is sufficient to inform those skilled in the relevant art how to make and use the claimed invention.
3. Regarding normal control synovium as compared to a disease state, immunostaining performed on five normal synovial tissues obtained from individual patients with hip fracture showed that all proteins (WNT10B, FRP1 and β -catenin) were negatively stained in normal synovium as shown in the attached Fig.1.

4. The WNT family members are “upregulated” in the RA synovium because WNT signaling and WNT target gene expression are specifically in RA synovium; and because biological actions of WNT signaling are compatible with aggressive features of RA synovium, i.e., enhanced cell proliferation, tissue remodeling and angiogenesis, and production of inflammatory cytokine expression.

5. In peer reviewed article by scientific references, the WNT family members are described as being “upregulated” in the RA synovium in “Differential Expression of WNTs and FRPs in the synovium of rheumatoid arthritis and osteoarthritis”, *Biochem. And Biophys. Res. Comm.*, 345, Page 1615-1620 (2006) (copy attached).

6. The data in *Biochem. And Biophys. Res. Comm.*, shows a predominant expression of WNT10B by RT-PCR (5/7 cases) and immuno-staining (16/16 cases) in RA synovium contrasted negligible expression in OA synovium (2/7 cases by RT-PCR and 6/14 cases by immuno-staining).

7. Hence, it is clear that the WNT family members are “upregulated” in the RA synovium.

Further Declarant Kazushi IMAI sayeth:

I declare that all statements are made of my own knowledge and are true and that all statements are made on information and belief that are believed to be true and further, that any false statements so made are punishable by fine or imprisonment, or both, under Section 1001 of

Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

March 22, 07

Date



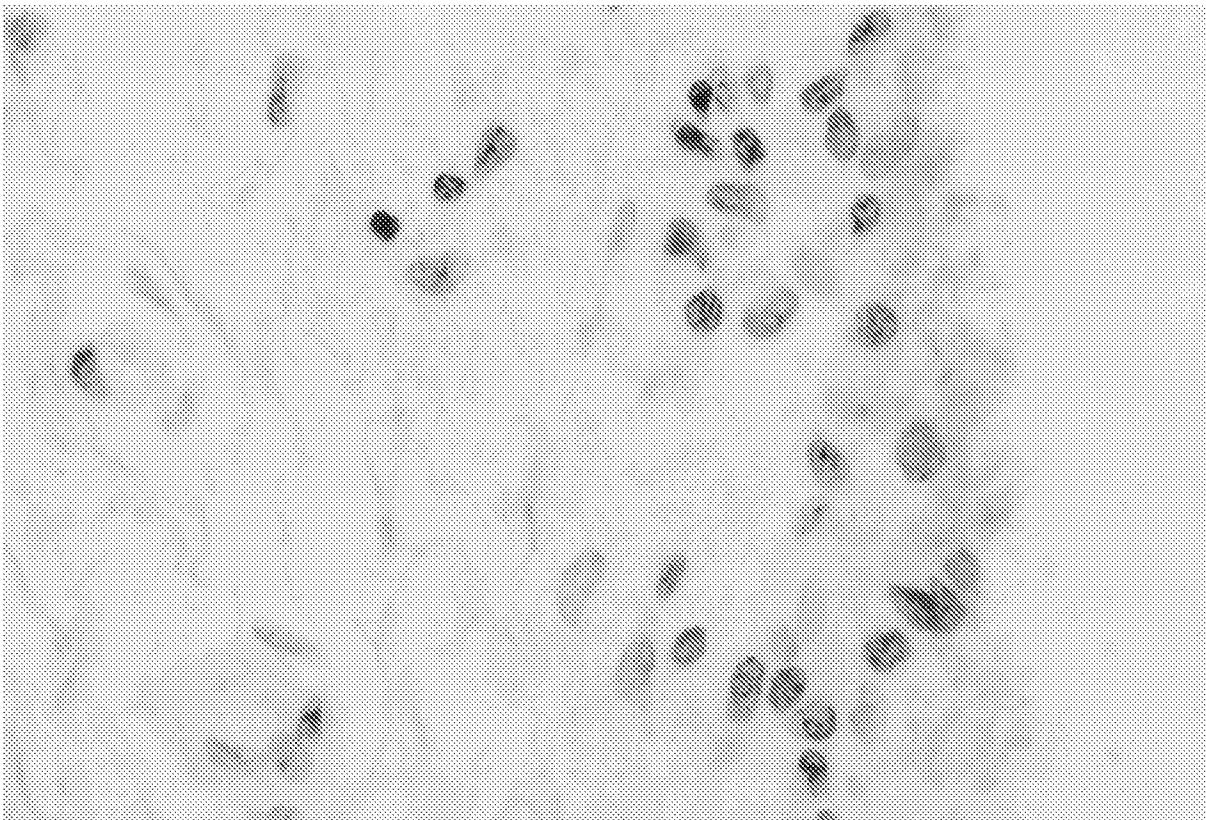
Kazushi IMAI

Fig. 1

WNT10B



FRP1



Normal synovium